PCT/US2004/035874

28 October 2004

29 October 2003

Amendments to the Specification:

Please replace the following heading and paragraph as the first paragraph on the first page in the application with the following amended paragraph:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a 371 National Phase Entry Application of co-pending International Application PCT/US2004/035874, filed October 28, 2004, which designated the U.S. and the present application claims benefit under 35 U.S.C §119(e) of U.S. Provisional Application No. 60/515,254, filed October 29, 2003; the contents of which are herewith incorporated by reference in their entirety.

Please replace paragraph [0082] with the following amended paragraph:

[0082] RNA isolated from cultured HUVEC, skin and heart samples, using the Ultraspec RNA Isolation System (Biotecx Laboratories, Houston, TX), was reverse transcribed and PCR was performed using standard techniques (12). Sequence-specific primers for PCR were human VEGF (sense primer 5'TCACCGCCTCGGCTTGTCACA-3' (SEQ ID NO:23), antisense primer 5'-ATGAACTTTCTGCTGTCTTGG-3' (SEQ ID NO:3)) and β-actin (Stratagene, La Jolla, CA) was used as an internal control. PCR reactions were performed under the following conditions: 1 cycle at 94 °C for 5 minutes followed by 35 cycles at 94 °C for 1 minute, 60 °C for 1 minute, and 72 °C for 1 minute. The last cycle was extended to 7 minutes at 72 °C. The amplified products were resolved by electrophoresis in an ethidium bromide-stained 1.5% agarose gel.

Please replace paragraph [00101] with the following amended paragraph:

[00101] Development of a blocking monoclonal antibody to VEGF: Rat antimouse VEGF monoclonal antibodies were generated using the N-terminal sequence of secreted VEGF: CAPTTEGEQKSHEVIKFMDVYQRSY (SEQ ID NO: 1) coupled with keyhole limpet hemocyanin (KLH) using the maleimidobenzyl-N-hydroxylsuccinimide ester (MBS) crosslinker. Fischer and Noble rats were immunized and hybridoma fusion products generated according to standard protocols. Fusion products were then chosen for scale up based their anti-VEGF OD reading in ELISA. The fusion from 300326 accession (Fisher rats) yielded 53 fusion products and the fusion from 300329 accession (Noble rats) yielded 15 fusion products. All chosen fusion products were scaled up, cryopreserved and screened again to confirm antibody production and the class of the specific antibody if present. The results

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of the secondary screens of the Noble rats demonstrated that there were 6 positives out 15 hopefuls, and 3 out of those 6 were strong IgG's. These were subcloned and scaled up and tested for VEGF neutralizing potential. We found that one lead antibody, called 2G11 had VEGF blocking ability in an in vitro endothelial cell proliferation assay.